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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 02	STN pricing information for 2008 now available
NEWS	3	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	4	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	5	JAN 28	MARPAT searching enhanced
NEWS	6	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	7	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	8	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	9	FEB 08	STN Express, Version 8.3, now available
NEWS	10	FEB 20	PCI now available as a replacement to DPCI
NEWS	11	FEB 25	IFIREF reloaded with enhancements
NEWS	12	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS	13	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification
NEWS	14	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	15	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	16	MAR 31	CA/CAplus and CASREACT patent number format for U.S. applications updated
NEWS	17	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	18	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	19	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	20	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	21	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	22	APR 28	IMSRESEARCH reloaded with enhancements

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 01:36:11 ON 08 MAY 2008

=> index bioscience medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE,
       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
       DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 01:36:38 ON 08 MAY 2008

72 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s gene?(s)target?(s)(recombinas? or endonucleas? or nucleas? or zinc?)
         26   FILE ADISINSIGHT
          9   FILE ADISNEWS
        368   FILE AGRICOLA
         15   FILE ANABSTR
         13   FILE ANTE
          6   FILE AQUALINE
         58   FILE AQUASCI
        677   FILE BIOENG
        661   FILE BIOSIS
       1838   FILE BIOTECHABS
       1838   FILE BIOTECHDS
  12 FILES SEARCHED...
       1942   FILE BIOTECHNO
        603   FILE CABA
       1467   FILE CAPLUS
         50   FILE CEABA-VTB
         18   FILE CIN
         12   FILE CONFSCI
          4   FILE CROPU
         65   FILE DDFU
  22 FILES SEARCHED...
      74883   FILE DGENE
  23 FILES SEARCHED...
        383   FILE DISSABS
        136   FILE DRUGU
          8   FILE EMBAL
        530   FILE EMBASE
       2812   FILE ESBIOBASE
  30 FILES SEARCHED...
         18   FILE FROSTI
         53   FILE FSTA
        411   FILE GENBANK
          7   FILE HEALSAFE
       1311   FILE IFIPAT
         45   FILE IMSDRUGNEWS
         25   FILE IMSRESEARCH
         15   FILE KOSMET
       2522   FILE LIFESCI
        591   FILE MEDLINE
         51   FILE NTIS
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         2   FILE NUTRACEUT
        10   FILE OCEAN
       924   FILE PASCAL
  47 FILES SEARCHED...
         2   FILE PHAR
         3   FILE PHARMAML
        27   FILE PHIN
       314   FILE PROMT
       655   FILE SCISEARCH
         3   FILE SYNTHLINE
       356   FILE TOXCENTER
      7702   FILE USGENE
  60 FILES SEARCHED...
     11946   FILE USPATFULL
        43   FILE USPATOLD
      1592   FILE USPAT2
        11   FILE WATER
       815   FILE WPIDS
        19   FILE WPIFV
       815   FILE WPINDEX
         7   FILE IPA
       193   FILE NLDB

  56 FILES HAVE ONE OR MORE ANSWERS,   72 FILES SEARCHED IN STNINDEX

L1   QUE GENE?(S) TARGET?(S)(RECOMBINAS? OR ENDONUCLEAS? OR NUCLEAS? OR ZINC?)

=> d rank
F1       74883   DGENE
F2       11946   USPATFULL
F3        7702   USGENE
F4        2812   ESBIOBASE
F5        2522   LIFESCI
F6        1942   BIOTECHNO
F7        1838   BIOTECHABS
F8        1838   BIOTECHDS
F9        1592   USPAT2
F10       1467   CAPLUS
F11       1311   IFIPAT
F12        924   PASCAL
F13        815   WPIDS
F14        815   WPINDEX
F15        677   BIOENG
F16        661   BIOSIS
F17        655   SCISEARCH
F18        603   CABA
F19        591   MEDLINE
F20        530   EMBASE
F21        411   GENBANK
F22        383   DISSABS
F23        368   AGRICOLA
F24        356   TOXCENTER
F25        314   PROMT
F26        193   NLDB
F27        136   DRUGU
F28         65   DDFU
F29         58   AQUASCI
F30         53   FSTA
F31         51   NTIS
F32         50   CEABA-VTB
F33         45   IMSDRUGNEWS
F34         43   USPATOLD
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F35         27   PHIN
F36         26   ADISINSIGHT
F37         25   IMSRESEARCH
F38         19   WPIFV
F39         18   CIN
F40         18   FROSTI
F41         15   ANABSTR
F42         15   KOSMET
F43         13   ANTE
F44         12   CONFSCI
F45         11   WATER
F46         10   OCEAN
F47          9   ADISNEWS
F48          8   EMBAL
F49          7   HEALSAFE
F50          7   IPA
F51          6   AQUALINE
F52          4   CROPU
F53          3   PHARMAML
F54          3   SYNTHLINE
F55          2   NUTRACEUT
F56          2   PHAR


=> file f2f-19
'F2F-19' IS NOT A VALID F# RANGE
SESSION CONTINUES IN INDEX FILES 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR,
ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS,
DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, FOMAD, FOREGE, FROSTI, FSTA,
GENBANK, HEALSAFE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IMSRESEARCH, KOSMET,
LIFESCI, MEDLINE, NTIS, NUTRACEUT, OCEAN, PASCAL, PCTGEN, PHAR, PHARMAML, PHIC,
PHIN, PROMT, PROUSDDR, PS, RDISCLOSURE, SCISEARCH, SYNTHLINE, TOXCENTER, USGENE,
USPATFULL, USPATOLD, USPAT2, VETB, VETU, WATER, WPIDS, WPIFV, WPINDEX, IPA,
NAPRALERT, NLDB'

=> file f2-f19
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   5.20       5.41

FILE 'USPATFULL' ENTERED AT 01:41:10 ON 08 MAY 2008
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FILE 'MEDLINE' ENTERED AT 01:41:10 ON 08 MAY 2008

=> s gene?(s)target?(s)(recombinas? or endonucleas? or nucleas? or zinc?)
   3 FILES SEARCHED...
   8 FILES SEARCHED...
  10 FILES SEARCHED...
L2       38060 GENE?(S) TARGET?(S)(RECOMBINAS? OR ENDONUCLEAS? OR NUCLEAS? OR
               ZINC?)

=> s l2(s)fok?(s)bindin?
L3          89 L2(S) FOK?(S) BINDIN?

=> dup rem l3
DUPLICATE IS NOT AVAILABLE IN 'USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L3
L4           60 DUP REM L3 (29 DUPLICATES REMOVED)

=> d ti l4

L4   ANSWER 1 OF 60  USPATFULL on STN
TI     GENETIC MODELS FOR STRATIFICATION OF CANCER RISK


=> d ti l4 1-60

L4   ANSWER 1 OF 60  USPATFULL on STN
TI     GENETIC MODELS FOR STRATIFICATION OF CANCER RISK
```

L4 ANSWER 2 OF 60 USPATFULL on STN DUPLICATE 1
TI Methods and compositions for targeted cleavage and recombination

L4 ANSWER 3 OF 60 USPATFULL on STN DUPLICATE 2
TI ZINC FINGER DOMAINS SPECIFICALLY BINDING AGC

L4 ANSWER 4 OF 60 USPATFULL on STN DUPLICATE 3
TI Targeted integration and expression of exogenous nucleic acid sequences

L4 ANSWER 5 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI New protein comprising an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions, useful in preparing a composition for treating or preventing HIV infection;
involving recombinant zinc finger protein DNA-binding domain useful for preparing pharmaceutical composition for the treatment of HIV infection

L4 ANSWER 6 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI New zinc finger nucleotide binding polypeptide, useful in preparing a composition for inhibiting the replication of HIV-1 virus;
involving vector-mediated gene transfer and expression in host cell for use in HIV virus-1 infection therapy and gene therapy

L4 ANSWER 7 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Cleaving target gene, e.g. cystic fibrosis transmembrane conductance regulator gene, in cell, comprises contacting cell with fusion protein having zinc finger binding domain and FokI cleavage domain, to cleave the mutated target gene;
cystic fibrosis transmembrane conductance regulator gene cleavage using non-homologous end-joining for gene correction and gene therapy

L4 ANSWER 8 OF 60 USPATFULL on STN
TI GENERATION OF ANIMAL MODELS

L4 ANSWER 9 OF 60 USPATFULL on STN
TI ZINC FINGER BINDING DOMAINS FOR TNN

L4 ANSWER 10 OF 60 USPATFULL on STN
TI Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site

L4 ANSWER 11 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Expressing product of exogenous nucleic acid sequence, by contacting cell having expressed fusion proteins of zinc finger binding domains, cleavage half-domain, with exogenous sequence, nucleotide sequence homology to first sequence;
involving use of RNA interference for a beta-thalassemia, chronic granulomatous diseases, cri du chat syndrome, cystic fibrosis, Gaucher disease, leukodystrophy, nephrogenic diabetes insipidus, Wilson's disease, Tay-Sach disease, Hunter disease, inherited disorder, cancer, ischemia, diabetic retinopathy, macular degeneration, rheumatoid arthritis, psoriasis, HIV virus infection, Alzheimer disease and stroke gene therapy application

L4 ANSWER 12 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE
TI The DNA binding domain of a papillomavirus E2 protein programs a chimeric nuclease to cleave integrated human papillomavirus DNA in HeLa cervical carcinoma cells

L4 ANSWER 13 OF 60 LIFESCI COPYRIGHT 2008 CSA on STN
TI Establishment of HIV-Resistant CD4 T Cells by Engineered Zinc Finger Protein Nucleases

L4 ANSWER 14 OF 60 LIFESCI COPYRIGHT 2008 CSA on STN
TI Targeted Killing of Glioblastoma Multiforme In Vivo by IL-13-Zetakine Redirected CTLs Made Glucocorticoid Resistant with Zinc Finger Nucleases

L4 ANSWER 15 OF 60 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Targeted killing of glioblastoma multiforme in vivo by IL-13 zetakine redirected CTLs made glucocorticoid resistant with zinc finger nucleases.

L4 ANSWER 16 OF 60 BIOENG COPYRIGHT 2008 CSA on STN
TI Establishment of HIV-Resistant CD4 T Cells by Engineered Zinc Finger Protein Nucleases

L4 ANSWER 17 OF 60 BIOENG COPYRIGHT 2008 CSA on STN
TI Targeted Killing of Glioblastoma Multiforme In Vivo by IL-13-Zetakine Redirected CTLs Made Glucocorticoid Resistant with Zinc Finger Nucleases

L4 ANSWER 18 OF 60 USPATFULL on STN
TI Custom-made meganuclease and use thereof

L4 ANSWER 19 OF 60 USPATFULL on STN
TI Targeted deletion of cellular DNA sequences

L4 ANSWER 20 OF 60 USPATFULL on STN
TI Use of meganucleases for inducing homologous recombination ex vivo and in toto in vertebrate somatic tissues and application thereof

L4 ANSWER 21 OF 60 IFIPAT COPYRIGHT 2008 IFI on STN
TI METHODS OF GENERATING ANTIBODY DIVERSITY IN VITRO

L4 ANSWER 22 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE
TI Mammalian gene targeting with designed zinc finger nucleases

L4 ANSWER 23 OF 60 USPATFULL on STN DUPLICATE 9
TI Genomics applications for modified OLIGO nucleotides

L4 ANSWER 24 OF 60 USPATFULL on STN DUPLICATE 10
TI Methods and compositions for targeted cleavage and recombination

L4 ANSWER 25 OF 60 USPATFULL on STN DUPLICATE 11
TI Use of chimeric nucleases to stimulate gene targeting

L4 ANSWER 26 OF 60 USPATFULL on STN
TI Novel lentiviral vectors for site-specific gene insertion

L4 ANSWER 27 OF 60 USPATFULL on STN
TI In vivo ssdna expression vectors for altering gene expression

L4 ANSWER 28 OF 60 USPATFULL on STN
TI Gene regulation II

L4 ANSWER 29 OF 60 USPATFULL on STN
TI Targeted chromosomal mutagenasis using zinc finger nucleases

L4 ANSWER 30 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Cleaving cellular chromatin in a region of interest, comprises engineering and expressing fusion proteins having zinc finger binding

domains binding to nucleotide sequence in region of interest and cleavage half domains, in a cell;
vector-mediated gene transfer and expression in host cell for recombinant zinc finger protein fusion protein production for use in gene therapy

L4 ANSWER 31 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Cleaving cellular chromatin in a region of interest, useful for preventing or treating cancer, diabetic retinopathy, sickle cell anemia, cystic fibrosis, Gaucher's disease, or hemophilias, comprises engineering zinc finger binding domain;
vector-mediated zinc finger protein domain gene transfer and expression in host cell for use in disease prevention and gene therapy

L4 ANSWER 32 OF 60 IFIPAT COPYRIGHT 2008 IFI on STN
TI TRUNCATION SELEX METHOD; DETECTION OF PREFERENTIAL NUCLEIC ACID LIGANDS; OBTAIN NUCLEOTIDE SEQUENCES, INCUBATE WITH OLIGONUCLEOTIDES, HYBRIDIZE, AMPLIFY, RECOVER NUCLEOTIDE SEQUENCES

L4 ANSWER 33 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE
TI Binding of two zinc finger nuclease monomers to two specific sites is required for effective double-strand DNA cleavage

L4 ANSWER 34 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Indexing double-stranded nucleic acid fragments from mixture, comprises treating with restriction endonuclease to generate fragments with protruding single strand, ligating C-indexer to fragments, obtaining circular indexed nucleic acid;
ds DNA fragment indexing for use in DNA amplification and mapping

L4 ANSWER 35 OF 60 USPATFULL on STN
TI Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site

L4 ANSWER 36 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI New chimeric nuclease comprising a DNA binding domain, a cleavage domain and a nuclear localization signal, useful in preparing a composition for treating or preventing a genetic disease e.g., hemophilia or Huntington's disease;
vector-mediated DNA binding protein gene transfer and expression in host cell for recombinant vaccine

L4 ANSWER 37 OF 60 USPAT2 on STN
TI Electrochemical sensor using intercalative, redox-active moieties

L4 ANSWER 38 OF 60 USPATFULL on STN DUPLICATE 14
TI Multiplexed systems for nucleic acid sequencing

L4 ANSWER 39 OF 60 USPATFULL on STN DUPLICATE 15
TI Mass labels

L4 ANSWER 40 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Targeted genetic recombination in a host cell comprises introducing into a host cell a nucleic acid molecule encoding a Zinc Finger Nuclease (ZFN), inducing expression of the ZFN, and identifying a host cell exhibiting a mutation;
vector-mediated zinc finger nuclease gene transfer and expression in plant or animal host cell for gene therapy or agriculture

L4 ANSWER 41 OF 60 USPATFULL on STN
TI Methods and compositions for using zinc finger endonucleases to enhance

homologous recombination

L4 ANSWER 42 OF 60 USPATFULL on STN
TI Tissues or organs for use in xenotransplantation

L4 ANSWER 43 OF 60 USPATFULL on STN
TI Tissues or organs for use in xenotransplantation

L4 ANSWER 44 OF 60 USPATFULL on STN
TI Genetically modified cows having reduced susceptibility to mad cow disease

L4 ANSWER 45 OF 60 USPATFULL on STN
TI Characterizing DNA

L4 ANSWER 46 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Cleaving target nucleic acid in cell with chimeric guide- endonuclease fusion molecule, by permitting the fusion molecule to cleave the target nucleic acid in the cell comprising the target and fusion molecules;
DNA cleavage and polymerase chain reaction useful for protein-interaction and drug screening

L4 ANSWER 47 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Enriching preselected nucleic acid segment encompassing specific variant at given position, from mixture of nucleic acids, comprises cleaving nucleic acids in mixture, selectively modifying the segment and enriching sample;
DNA and RNA segment enhancement useful for DNA analysis and mutation detection

L4 ANSWER 48 OF 60 USPAT2 on STN
TI Nuclease

L4 ANSWER 49 OF 60 IFIPAT COPYRIGHT 2008 IFI on STN
TI TRUNCATION SELEX METHOD; DETECTION OF PREFERENTIAL NUCLEIC ACID LIGANDS; OBTAIN NUCLEOTIDE SEQUENCES, INCUBATE WITH OLIGONUCLEOTIDES, HYBRIDIZE, AMPLIFY, RECOVER NUCLEOTIDE SEQUENCES

L4 ANSWER 50 OF 60 USPATFULL on STN DUPLICATE 17
TI Method of regulating transcription in a cell

L4 ANSWER 51 OF 60 USPATFULL on STN
TI Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site

L4 ANSWER 52 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI Producing sequence variations in DNA, useful for preparing optimized proteins, comprises inserting a transposon and then targeted but incomplete removal of the transposon;
using restriction endonuclease, black gram bean nuclease and DNA-ase for protein engineering for use in disease diagnosis and therapy

L4 ANSWER 53 OF 60 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
TI Chimeric Nucleases Stimulate Gene Targeting in Human Cells.

L4 ANSWER 54 OF 60 CAPLUS COPYRIGHT 2008 ACS on STN
TI Molecular switches II system comprising ligand-regulated DNA binding molecule and targeted DNA binding site and its use in screening for desired binding elements and gene regulation

L4 ANSWER 55 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.

on STN DUPLICATE
TI Long-range identification of hepatocyte nuclear factor-3 (FoxA) high and low-affinity binding sites with a chimeric nuclease

L4 ANSWER 56 OF 60 CAPLUS COPYRIGHT 2008 ACS on STN
TI Gene repair involving homologous recombination induced by in vivo double-stranded cleavage of targeting DNA mediated by chimeric restriction endonuclease

L4 ANSWER 57 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.
on STN DUPLICATE
TI Chimeric restriction enzymes: What is next?

L4 ANSWER 58 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.
on STN DUPLICATE
TI APETALA3-nuclease hybrid protein: A potential tool for APETALA3 target gene mutagenesis

L4 ANSWER 59 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
TI New chimeric protein containing two or more polypeptide binding domains; DNA binding protein gene transfer for use as a transcription activator, repressor or in DNA cleavage, for gene therapy, transgenic animal construction, etc.

L4 ANSWER 60 OF 60 IFIPAT COPYRIGHT 2008 IFI on STN
TI STRAND DISPLACEMENT AMPLIFICATION; GENETIC ENGINEERING

=> d ibib abs l4 2-7,10,15,18-20,22,26-27,35-36,40-41,51,53,56

L4 ANSWER 2 OF 60 USPATFULL on STN DUPLICATE 1
ACCESSION NUMBER: 2007:249892 USPATFULL
TITLE: Methods and compositions for targeted cleavage and recombination
INVENTOR(S): Miller, Jeffrey C., San Francisco, CA, UNITED STATES
PATENT ASSIGNEE(S): Sangamo BioSciences, Inc., Richmond, CA, UNITED STATES, 94804 (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007218528	A1	20070920	
APPLICATION INFO.:	US 2005-587723	A1	20050203	(10)
	WO 2005-US3245		20050203	
			20070425	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-542780P	20040205 (60)
	US 2004-556831P	20040326 (60)
	US 2004-575919P	20040601 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROBINS & PASTERNAK, 1731 EMBARCADERO ROAD, SUITE 230, PALO ALTO, CA, 94303, US
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 45 Drawing Page(s)
LINE COUNT: 5209
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein are methods and compositions for targeted cleavage of a genomic sequence, targeted alteration of a genomic sequence, and targeted recombination between a genomic region and an exogenous

polynucleotide homologous to the genomic region. The compositions include fusion proteins comprising a cleavage domain (or cleavage half-domain) and an engineered zinc finger domain, as well as polynucleotides encoding same. Fusion proteins comprising cleavage half-domains are used in pairs, to reconstitute a functional cleavage domain. In these fusion proteins, the zinc finger domain can be N-terminal to the cleavage half-domain, or the cleavage half-domain can be N-terminal to the zinc finger domain. The availability of fusion endonucleases having these different polarities allows targeting (and thereby binding) of zinc finger endonucleases either to opposite strands of the DNA target or to the same strand of the DNA target, thereby increasing the number of possible sequences which can be targeted and cleaved by the fusion proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 3 OF 60 USPATFULL on STN DUPLICATE 2
ACCESSION NUMBER: 2007:177172 USPATFULL
TITLE: ZINC FINGER DOMAINS SPECIFICALLY BINDING AGC
INVENTOR(S): Barbas, Carlos F. III, Solana Beach, CA, UNITED STATES
PATENT ASSIGNEE(S): The Scripps Research Institute, La Jolla, CA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007154989	A1	20070705	
APPLICATION INFO.:	US 2006-613075	A1	20061219	(11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2006-756083P	20060103 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CATALYST LAW GROUP, APC, 9710 SCRANTON ROAD, SUITE S-170, SAN DIEGO, CA, 92121, US
NUMBER OF CLAIMS: 82
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 4061
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polypeptides that contain zinc finger-nucleotide binding regions that bind to nucleotide sequences of the formula AGC are provided. Compositions containing a plurality of polypeptides, isolated heptapeptides possessing specific binding activity, polynucleotides that encode such polypeptides and methods of regulating gene expression with such polypeptides, compositions and polynucleotides are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 60 USPATFULL on STN DUPLICATE 3
ACCESSION NUMBER: 2007:154580 USPATFULL
TITLE: Targeted integration and expression of exogenous nucleic acid sequences
INVENTOR(S): Holmes, Michael C., Oakland, CA, UNITED STATES
Urnov, Fyodor, Point Richmond, CA, UNITED STATES
Gregory, Philip D., Orinda, CA, UNITED STATES
Rebar, Edward J., El Cerrito, CA, UNITED STATES
Brennan, Sean M., San Ramon, CA, UNITED STATES
PATENT ASSIGNEE(S): Sangamo BioSciences, Inc. (U.S. corporation)

	NUMBER	KIND	DATE

PATENT INFORMATION: US 2007134796 A1 20070614
APPLICATION INFO.: US 2006-493423 A1 20060726 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-702394P	20050726 (60)
	US 2005-721054P	20050926 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROBINS & PASTERNAK, 1731 EMBARCADERO ROAD, SUITE 230, PALO ALTO, CA, 94303, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 54 Drawing Page(s)
LINE COUNT: 7437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed herein are methods and compositions for targeted integration of a exogenous sequence into a predetermined target site in a genome for use, for example, in protein expression and gene inactivation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 5 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
DUPLICATE 4
ACCESSION NUMBER: 2008-01245 BIOTECHDS
TITLE: New protein comprising an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions, useful in preparing a composition for treating or preventing HIV infection;
involving recombinant zinc finger protein DNA-binding domain useful for preparing pharmaceutical composition for the treatment of HIV infection
AUTHOR: ANDO D; HOLMES M C; LEE G K L
PATENT ASSIGNEE: SANGAMO BIOSCIENCES INC
PATENT INFO: WO 2007139982 6 Dec 2007
APPLICATION INFO: WO 2007-US12588 23 May 2007
PRIORITY INFO: US 2007-926911 30 Apr 2007; US 2006-808501 25 May 2006
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2008-A18635 [01]
AN 2008-01245 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - A new protein comprises an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions.

DETAILED DESCRIPTION - The new protein comprises an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions comprising: Asp-Arg-Ser-Asn-Leu-Ser-Arg; Ile-Ser-Ser-Asn-Leu-Asn-Ser or Val-Ser-Ser-Asn-Leu-Thr-Ser; Arg-Ser-Asp-Asn-Leu-Ala-Arg; or Thr-Ser-Gly-Asn-Leu-Thr-Arg (SEQ ID NO: not defined). INDEPENDENT CLAIMS are: (1) a polynucleotide encoding the protein; (2) a gene delivery vector comprising the polynucleotide; (3) an isolated cell comprising the protein or the polynucleotide; (4) a method for inactivating the CCR-5 gene in a human cell by administering to the cell the protein, the polynucleotide or the gene delivery vector; and (5) a method for treating or preventing HIV infection in a subject.

BIOTECHNOLOGY - Preferred Protein: The protein comprises an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions comprising: Asp-Arg-Ser-Asn-Leu-Ser-Arg; Ile-Ser-Ser-Asn-Leu-Asn-Ser or Val-Ser-Ser-Asn-Leu-Thr-Ser; Arg-Ser-Asp-Asn-Leu-Ala-Arg; or

Thr-Ser-Gly-Asn-Leu-Thr-Arg (SEQ ID NO: not defined). The protein further comprises a cleavage domain. The cleavage domain is a cleavage half-domain. The cleavage half-domain is a wild-type FokI cleavage half-domain. The cleavage half-domain is an engineered FokI cleavage half-domain. Preferred Vector: The gene delivery vector is an adenovirus vector, preferably Ad5/35 vector. Preferred Cell: The cell is a hematopoietic stem cell, a T-cell, a macrophage, a dendritic cell or an antigen-presenting cell. The T-cell is a CD4+ cell. The cell is a K562 cell, a HEK293 cell, a PM-1, a THP-1 cell or a GHOST cell line. Preferred Method: Treating or preventing HIV infection in a subject comprises: (a) introducing, into a cell, a first nucleic acid encoding a first polypeptide, where the first polypeptide comprises a zinc finger DNA-binding domain that is engineered to bind to a first target site in the CCR-5 gene and a cleavage domain; such that the polypeptide is expressed in the cell, where the polypeptide binds to the target site and cleaves the CCR-5 gene; and (b) introducing the cell into the subject. The nucleic acid comprises the polynucleotide. The first nucleic acid further encodes a second polypeptide comprising (i) a zinc finger DNA-binding domain that is engineered to bind to a second target site in the CCR-5 gene, and (ii) a cleavage domain; such that the second polypeptide is expressed in the cell, where the first and second polypeptides bind to their respective target sites and cleave the CCR-5 gene.
The method further comprises introducing into the cell a second nucleic acid containing two regions of homology to the CCR-5 gene, flanking a sequence that is non-homologous to the CCR-5 gene.

ACTIVITY - Anti-HIV. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The protein comprising an engineered zinc finger protein DNA-binding domain comprising four zinc finger recognition regions is useful in gene modification, gene correction, and gene disruption or in preparing a composition for treating or preventing HIV infection in a subject.

EXAMPLE - No suitable example given.(76 pages)

L4 ANSWER 6 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2007-18272 BIOTECHDS
TITLE: New zinc finger nucleotide binding polypeptide, useful in preparing a composition for inhibiting the replication of HIV-1 virus;
involving vector-mediated gene transfer and expression in host cell for use in HIV virus-1 infection therapy and gene therapy
AUTHOR: BARBAS C F; DREIER B
PATENT ASSIGNEE: SCRIPPS RES INST
PATENT INFO: WO 2007062422 31 May 2007
APPLICATION INFO: WO 2006-US61289 28 Nov 2006
PRIORITY INFO: US 2005-740525 28 Nov 2005; US 2005-740525 28 Nov 2005
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2007-526353 [51]
AN 2007-18272 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A new isolated and purified zinc finger nucleotide binding polypeptide comprises a nucleotide binding region of 5 to 10 amino acid residues.

DETAILED DESCRIPTION - The new isolated and purified zinc finger nucleotide binding polypeptide comprises a nucleotide binding region of 5 to 10 amino acid residues. The region binds preferentially to a target nucleotide of the formula TNN, where

N is A, C, G or T. INDEPENDENT CLAIMS are: (1) a polypeptide composition; (2) an isolated and purified polynucleotide that encodes the polypeptide, the polypeptide composition or the isolated heptapeptide; (3) a vector comprising the isolated and purified polynucleotide; (4) a host cell transformed or transfected with the vector; (5) a process of regulating expression of a nucleotide sequence that contains the sequence 5'-(TNN)-3', where n is 2 to 12; (6) a method of inhibiting the replication of HIV-1 virus by administering to an individual infected with HIV-1 virus a sufficient quantity of the artificial transcription factor capable of binding to the tRNA primer-binding site such that replication of HIV-1 is inhibited; (7) a pharmaceutical composition; and (8) a method for inhibiting the replication of HIV-1 virus by administering to an individual infected with HIV-1 virus a sufficient quantity of a polynucleotide encoding the artificial transcription factor.

BIOTECHNOLOGY - Preferred Polypeptide: The isolated and purified zinc finger nucleotide binding polypeptide comprises a nucleotide binding region of 5 to 10 amino acid residues. The region binds preferentially to a target nucleotide of the formula TNN, where N is A, C, G or T. The target nucleotide has the formula TAN, TCN, TGN, TTN, TNA, TNC, TNG or TNT. The target nucleotide has the formula TAA, TAG, TAG, TAT, TOA, TOC, TCG, TGT, TGA, TGC, TGG, TGT, HA, TTC, TTG or TTT. The binding region has an amino acid sequence with the same nucleotide binding characteristics as SEQ ID NO: 1-411. The binding region has an amino acid sequence with the same nucleotide binding characteristics as any of SEQ ID NO: 1-46. The binding region has an amino acid sequence with the same nucleotide binding characteristics as SEQ ID NO: 1-6. The binding region competes for binding with a polypeptide that includes SEQ ID NO: 1-411, 1-46 or 1-6. The binding region has SEQ ID NO: 1-411, 1-46 or 1-6. The nucleotide binding region is 7 residues and has alpha-helical structure. The binding region has an amino acid sequence consisting of: (a) the binding region of the amino acid sequence of any of SEQ ID NO: 1 through SEQ ID NO: 411; and (b) a binding region, differing from the amino acid sequence of any of SEQ ID NO: 1 through SEQ ID NO: 411 by no more than two conservative amino acid substitutions, where the dissociation constant is no greater than 125% of that of the polypeptide before the substitutions are made, and where a conservative amino acid substitution is one of the following substitutions: Ala/Gly or Ser; Arg/Lys; Asn/Gln or His; Asp/Glu; Cys/Ser; Gln/Met; Gly/Asp; Gly/Ala or Pro; His/Met or Gln; Ile/Leu or Val; Leu/Ile or Val; Lys/Arg or Gln or Glu; Met/Leu or Tyr or Ile; Phe/Met or Leu or Tyr; Ser/Thr; Thr/Ser; Trp/Tyr; Tyr/Trp or Phe; Val/Ile or Leu. The binding region differs from the amino add sequence of SEQ ID NO: 1 through SEQ ID NO: 411 by no more than one conservative amino acid substitution. The binding region differs from the amino acid sequence of any of SEQ ID NO: 1 through SEQ ID NO: 46 by no more than two conservative amino acid substitutions. The binding region differs from the amino acid sequence of any of SEQ ID NO: 1 through SEQ ID NO: 46 by no more than one conservative amino acid substitution. The binding region differs from the amino acid sequence of any of SEQ ID NO: 1 through SEQ D NO: 6 by no more than two conservative amino acid substitutions. The binding region differs from the amino acid sequence of any of SEQ ID NO: 1 through SEQ ID NO: 6 by no more than one conservative amino acid substitution. The nucleotide binding region comprises a 7-amino acid zinc finger domain in which the seven amino acids of the domain are numbered from 1 to 6. The domain is: (a) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TAA)-3', where the amino acid residue of the domain numbered -1 is Gln, Asn and Ser; (b) a zinc finger nucleotide binding domain specifically

binding the nucleotide sequence 5'-(TCA)-5', where the amino acid residue of the domain numbered -1 is Ser; (c) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-TNG-3', where N is A, C, G or T, where the amino acid residue of the domain numbered -1 is Arg, Asn, Gln, His, Ser, Thr or Ile; (g) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TNC)-3', where N is any of A, C, G or T, where the amino acid residue numbered 2 of the domain is G; (h) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-TNT-3', where N is any of A, C, D, or T, where the amino acid residue of the domain numbered -1 is Arg, Asn, Gln, His, Thr, Ala or Cys; (i) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TNC)-S', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered -1 is Gln, Ser, Asn, Gly, His or Asp; (g) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TAN)-3', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered 3 is His, Asn, Asp, Val, Ile or Lys; (h) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TCN)-3', where N is any of A, C, G or T, where the amino acid residue of the domain numbered 3 is Thr, Asp, His, Lys or Asn; (i) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TCC)-3', where the amino acid residue of the domain numbered 3 is Asn, His, Ser, Asp, Thr, Gln or Gly; (j) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TCG)-3', where the amino acid residue of the domain numbered 3 is Thr, His, Ser, Asp, Asn, Gly or Cys; (k) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TGN)-3', where N is any of A, C, G or T, where the amino acid residue of the domain numbered 3 is His; (i) a zinc finger nucleotide binding domain specifically binding a nucleotide sequence selected from the group consisting of 5'-(TGG)-3' and 5'-(TGT)-3', where the amino acid residue of the domain numbered 3 is Thr, Asn, Asp or His; (m) a zinc finger nucleotide binding domain: specifically binding the nucleotide sequence 5'-(TGC)-3', where the amino acid residue of the domain numbered 3 is Trp, Thr or His; (n) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TGN)-3', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered 3 is His; (o) a zinc finger nucleotide binding domain specifically binding a nucleotide sequence consisting of 5'-TTA-3' and 5'-(TTG)-3', where the amino acid residue of the domain numbered 3 is Ser or Ala; (p) a zinc finger nucleotide binding domain specifically binding a nucleotide sequence selected from the group consisting of 5'-(TTC)-3' and 5'-(TTT)-3', where the amino acid residue of the domain numbered 3 is His; (q) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TNA)-3', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered -1 is Arg; (r) a zinc linger nucleotide binding domain specifically binding the nucleotide sequence 5'-(TNT)-3', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered -1 is Ser, Thr or His; and (s) a zinc finger nucleotide binding domain specifically binding the nucleotide sequence 5'-TNN-3', where N is any of A, C, G, or T, where the amino acid residue of the domain numbered 4 is Leu, Val, Ile or Cys. The polypeptide is derived from a polypeptide, where the nucleotide binding region is derived from a nucleotide binding region that is any of SEQ ID NO: 1 through SEQ ID NO: 411 through molecular modeling, such

that the hydrogen bonding pattern is similar to at least one of SEQ ID NO: 1 through SEQ ID NO: 411. The polypeptide is operatively linked to at least one other zinc finger nucleotide binding polypeptide binding preferentially to a target nucleotide of the formula ANN, CNN, or GNN, where N is A, C, G or T. The polypeptide is operatively linked to on or more transcription regulating factors. The polypeptide is operatively linked to one or more transcription regulating factors. The transcription, regulating factor is a repressor of transcription. The transcription regulating factor is an activator or a repressor of transcription. The transcription regulating factor is histone deacetylase or a modulator of histone deacetylase expression. The polypeptide is an artificial transcription factor that binds at least a portion of the HIV-1 tRNA primer-binding site. The artificial transcription factor has six zinc finger DNA-binding domains and has one zinc finger DNA binding domain that binds preferentially to a target nucleotide of the formula TNN, where N is A, C, G or T. The artificial transcription factor is assembled in a Sp1C zinc finger scaffold. The artificial transcription factor includes at least one KRAB repression domain. The polypeptide is a heptapeptide having an alpha-helical structure and that binds preferentially to a target nucleotide of the formula TNN, where N is A, C, G or T. Preferred Host Cell: The host cell is eukaryotic or prokaryotic. Preferred Polynucleotide: The polynucleotide comprises (a) an isolated and purified polynucleotide that encodes the polypeptide and (b) nucleic acid sequences that are at least 95% identical with the sequences of (a), provided that the nucleic acid sequences are translated into polypeptides that possess the activity of the polypeptide, including specific nucleic acid binding activity. The polynucleotide comprises (a) an isolated and purified polynucleotide that encodes the polypeptide composition and (b) nucleic acid sequences that are at least 95% identical with the sequences of (a), provided that the nucleic acid sequences are translated into polypeptides that possess the activity of the polypeptide composition, including specific nucleic acid binding activity. Preferred Composition: The polypeptide composition comprises the polypeptides of the invention operatively linked to each other. The polypeptides are operatively linked via a flexible peptide linker of 5 to 15 amino acid residues. The linker has a sequence consisting of SEQ ID NO: 412, 414, 416, 420, 417, 418, 419, 421 or 422. The polypeptide composition comprises from 2 to 18 polypeptides. The polypeptide composition comprises 2 to 12 polypeptides. The polypeptide composition binds to a nucleotide sequence that contains a sequence of the formula 5'-(TNN)n-3', where N is A, C, G or T and n is 2 to 12. The composition comprises 2 to 6 polypeptides. The composition binds to a nucleotide sequence that contains a sequence of the formula 5'-(TNN)n-3', where N is A, C, G or T and n is 2 to 6. The composition further comprises at least one polypeptide with a binding region that binds a nucleotide subsite of the sequence 5'-(ANN)-3', 5'-(CNN)-.3' or 5'-(GNN)-3'. The polypeptide composition is derived from a polypeptide composition, where the nucleotide binding region of each polypeptide is derived from a nucleotide binding region that is any of SEQ. ID NO: 1-411 through molecular modeling, such that the hydrogen bonding pattern is substantially similar to SEQ ID NO: 1-411. The polypeptide composition comprises a bispecific zinc finger protein comprising two halves, each half comprising six zinc finger nucleotide binding domains, where at least one of the halves includes at least one domain binding a target nucleotide sequence of the 5'-(TNN)-3', such that the two halves of the bispecific zinc fingers can operate independently. The two halves of the bispecific zinc finger protein are joined by a linker. The linker has the amino acid residue sequence Thr-Gly-Gly-Gly-Gly-Ser-Gly-Gly-Gly-Gly-Thr-Gly-Glu-Lys-Pro (SEQ

ID NO: 414). The polypeptide composition further comprises the nuclease catalytic domain of FokI such that the polypeptide composition directs site-specific cleavage at a chosen genomic target. The polypeptide composition is operatively linked to at least one other zinc finger nucleotide binding polypeptide binding preferentially to a target nucleotide of the formula ANN, CNN, or ONN, where N is A, C, G or T. The polypeptide composition is operatively linked to one or more transcription factors. The polypeptide composition is operatively linked to one or more transcription regulating factors. The pharmaceutical composition comprises the polypeptide, heptapeptide, polynucleotide, artificial transcription factor or polypeptide composition. The composition further comprises a carrier. Preferred Method: Regulating expression of a nucleotide sequence that contains the sequence 5'-(TNN)-3', where n is 2 to 12 comprises exposing the nucleotide sequence to an effective amount of the polypeptide composition. The sequence 5'-(TNN)-3' is located within a 5'-(TNN)n-3' sequence. The sequence 5'-(TNN)n-3' is located in the transcribed region of the nucleotide sequence. The sequence 5'-(TNN)n-3' is located in a promoter region of the nucleotide sequence. The sequence 5'-(TNN)n-3' is located within an expressed sequence tag. The nucleotide sequence is a eukaryotic or prokaryotic gene. The gene is a viral gene. The eukaryotic gene is a mammalian gene . The mammalian gene is a human gene. The eukaryotic gene is a plant gene. The prokaryotic gene is a bacterial gene.

ACTIVITY - Virucide. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The isolated and purified zinc finger nucleotide binding polypeptide is useful in preparing a composition for inhibiting the replication of HIV-1 virus.

ADMINISTRATION - The composition is administered via oral, subcutaneous, intravenous, intramuscular, intrasternal, infusion techniques, intraperitoneal administration or parenteral route. No dosage details given.

EXAMPLE - No suitable example given.(180 pages)

L4 ANSWER 7 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
DUPLICATE 6

ACCESSION NUMBER: 2007-06942 BIOTECHDS
TITLE: Cleaving target gene, e.g. cystic fibrosis transmembrane conductance regulator gene, in cell, comprises contacting cell with fusion protein having zinc finger binding domain and FokI cleavage domain, to cleave the mutated target gene;
cystic fibrosis transmembrane conductance regulator gene cleavage using non-homologous end-joining for gene correction and gene therapy
AUTHOR: CHANDRASEGARAN S
PATENT ASSIGNEE: UNIV JOHNS HOPKINS
PATENT INFO: WO 2007014181 1 Feb 2007
APPLICATION INFO: WO 2006-US28739 25 Jul 2006
PRIORITY INFO: US 2005-702260 25 Jul 2005; US 2005-702260 25 Jul 2005
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2007-176918 [17]
AN 2007-06942 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Cleaving a gene of interest in a cell, comprising providing a fusion protein comprising a zinc finger binding domain and a FokI cleavage domain, where the

zinc finger binding domain binds to a target site in the gene of interest, and contacting the cell with the fusion protein under conditions such that the gene of interest is cleaved, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition useful for disrupting cystic fibrosis transmembrane conductance regulator (CFTR), dystrophia myotonica protein kinase (DMPK), CC-chemokine receptor 5 (CCR5), or tyrosinase gene (TYR) in a cell, comprising an engineered fusion protein having a zinc finger binding domain to bind the CFTR, DMPK, CCR5, or TYR target sequence and a FokI cleavage domain, where the fusion protein binds to and cleaves the CFTR, DMPK, CCR5, or TYR gene.

BIOTECHNOLOGY - Preferred Method: The method further involves contacting the cell with a polynucleotide, where the polynucleotide replaces sequences in the cleaved gene of interest, where the gene of interest is CFTR, DMPK, CCR5, TYR or beta globin, and the zinc finger binding domain binds to a target site in the CFTR, DMPK, CCR5, TYR or beta globin genes, and the CFTR, DMPK, CCR5, TYR, or beta globin genes are cleaved. The replaced sequences of the gene of interest comprise a mutation associated with a disease or condition mediated by a mutant form of the gene of interest. The method further involves contacting the cell with a polynucleotide, where the polynucleotide replaces sequences in the cleaved CFTR, DMPK, CCR5, TYR or beta globin gene. The zinc finger binding domain comprises, as a recognition region, one of the six 7 amino acid sequences shown for mCFTR, hDMPK, hCCR5, or mTYR. The replaced sequences of CFTR gene comprise a mutation associated with cystic fibrosis. The replaced sequences of DMPK gene comprise a mutation associated with myotonic dystrophy. The replaced sequences comprise a mutation associated with CCR5. The replaced sequences of TYR gene comprise a mutation associated with TYR gene comprise a mutation associated with tyrosinase enzyme activity. The replaced sequences of beta globin gene comprise a mutation associated with beta globin gene comprise a mutation associated with sickle cell anemia. The zinc finger binding domain comprises three zinc fingers, where the recognition region of each of the three zinc fingers is ZF1, ZF2 or ZF3, or ZF4, ZF5 or ZF6. The CCR5 gene after cleavage is repaired by non-homologous end-joining in the cell to give rise to a CCR5 gene mutation that inactivates the CCR5 receptor. The replacing sequences comprise the CCR5delta 32 mutation, therefore inactivating the CCR5 receptor. The CCR5 chromosomal gene locus after cleavage serves as a safe harbor site within the human genome for introducing and ectopically expressing other human genes as transgenes in human cell types for human therapeutics. The replacing sequences encode a therapeutic protein or marker gene, where the marker gene is neomycin or green fluorescent protein (GFP). The zinc finger binding domain of mCFTR comprises sequences such as Gln-Ser-Ala-Asn-Leu-Ala-Arg, Gln-Ser-Gly-His-Leu-Thr-Arg, Arg-Ser-Asp-Ser-Leu-Thr-Lys, Gln-Ala-Gly-His-Leu-Ala-Ser, Arg-Ser-Asp-Asn-Leu-Ala-Arg, and Arg-Ser-Asp-Asn-Leu-Arg-Glu. The zinc finger binding domain of hDMPK comprises sequences such as Arg-Ser-Asp-Asn-Leu-Ala-Arg, Arg-Ser-Asp-His-Leu-Thr-Lys, Asp-Arg-Ser-Asp-Leu-Thr-Arg, Asp-Arg-Ser-His-Leu-Thr-Arg, Arg-Ser-Asp-Glu-Leu-Gln-Arg, and Arg-Ser-Asp-His-Leu-Ser-Arg. The zinc finger binding domain of hCCR5 comprises sequences such as Glu-Arg-Gly-Thr-Leu-Ala-Arg, Asp-Arg-Ser-Asp-Leu-Thr-Arg, Gln-Ser-Ser-Asp-Leu-Thr-Arg, Asp-Arg-Ser-Asn-Leu-Thr-Arg, Arg-Ser-Asp-His-Leu-Thr-Lys, and Gln-Ser-Ser-Asn-Leu-Ala-Arg. The zinc finger binding domain of mTYR comprises sequences such as Asp-Arg-Ser-Asn-Leu-Thr-Arg, Thr-Thr-Ser-Asn-Leu-Ala-Arg,

Arg-Ser-Asp-Ala-Leu-Thr-Arg, Gln-Ser-Ser-Asn-Leu-Ala-Arg, Arg-Ser-Asp-His-Leu-Thr-Lys, Gln-Ser-Ser-Asn-Leu-Ala-Arg, as given in table 1 of the patent specification.

ACTIVITY - CNS-Gen.; Respiratory-Gen.; Antianemic; Anti-HIV. No biological data given.

MECHANISM OF ACTION - Cleaves CFTR, DMPK, CCR5 or TYR genes ; Gene Therapy.

USE - For cleaving a gene of interest in a cell, where the gene of interest is CFTR associated with cystic fibrosis, DMPK associated with myotonic dystrophy, CCR5, TYR or beta globin associated with sickle cell anemia. The cell is a human cell, preferably human primary cell, human adult stem cell, human embryonic stem cell, human hematopoietic stem cell, human melanocyte or human stem cell, and the gene is a human gene (all claimed), which is useful in gene editing and/or gene correction, and in human therapeutics for treating HIV.

ADVANTAGE - The four-finger zinc finger chimeric endonuclease enables efficient and permanent alteration of gene encoding human interleukin-2 receptor.

EXAMPLE - Target disruption of CC-chemokine receptor-5 (CCR5) gene in human embryonic kidney (HEK)-293 Flp-In cells by mutagenic repair through non-homologous end-joining (NHEJ) was carried out as follows. CCR5 cDNA was cloned into an expression plasmid pcDNA/FRT/TO containing one Flp recognition target (FRT) site, tetracycline inducible promoter and hygromycin resistance gene, and was co-transfected with Flp recombinase expression plasmid pOG44 into the Flp-In HEK293 cells. The Flp recombinase mediates homologous recombination (HR) between the two FRT sites, and the pcDNA/FRT/TO construct was inserted into the genome at the integrated FRT site. Many individual clones resistant to CCR5 expression were analyzed by flow cytometry using phycoerythrin conjugated CCR5 antibody. The engineered zinc finger nuclease was transfected into CCR5 expressing HEK293 Flp-In cells. After 3-4 days of post-transfection the cells were analyzed for CCR5 expression. The CCR5 negative cells were found to be declined after four days of post-transfection with zinc finger nuclease. Results indicated that the engineered zinc finger nuclease induced directed mutations by NHEJ, at the CCR5 gene locus through targeted cleavage.(75 pages)

L4 ANSWER 10 OF 60 USPATFULL on STN

ACCESSION NUMBER:	2007:161485 USPATFULL
TITLE:	Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site
INVENTOR(S):	Choulika, Andre, Paris, FRANCE Mulligan, Richard C., Lincoln, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2007141038	A1	20070621
APPLICATION INFO.:	US 2006-636397	A1	20061208 (11)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2003-337229, filed on 6 Jan 2003, ABANDONED Continuation of Ser. No. US 2001-917295, filed on 27 Jul 2001, ABANDONED Continuation of Ser. No. WO 2000-US3014, filed on 3 Feb 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-118669P	19990203 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION

LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133, US
NUMBER OF CLAIMS: 52
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1122
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell are disclosed. Also disclosed are methods of treating or prophylaxis of a genetic disease in an individual in need thereof. Further disclosed are chimeric restriction endonucleases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 15 OF 60 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2008:217827 BIOSIS
DOCUMENT NUMBER: PREV200800217869
TITLE: Targeted killing of glioblastoma multiforme in vivo by IL-13 zetakine redirected CTLs made glucocorticoid resistant with zinc finger nucleases.
AUTHOR(S): Reik, Andreas [Reprint Author]; Holmes, Michael C.; Zhou, Yuanyue; Mendel, Matthew; Liu, Pei-Qi; Lee, Gary; Paschon, David.; Rebar, Edward; Ando, Dale; DiGiusto, David; Gregory, Philip D.; Jensen, Michael C.
CORPORATE SOURCE: Sangamo BioSci Inc, Richmond, CA USA
SOURCE: Blood, (NOV 16 2007) Vol. 110, No. 11, Part 1, pp. 765A. Meeting Info.: 49th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 08 -11, 2007. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Mar 2008
Last Updated on STN: 26 Mar 2008
AB Genetic modification of cytolytic T-lymphocytes (CTL) for enhancing their functional immunobiology is a promising immunotherapeutic approach for the treatment of cancer and infectious disease. CTLs modified to express a chimeric antigen receptor comprising an extracellular IL13 domain and cytoplasmic CD3 domain (IL13-zetakine) can be redirected both in vitro and in animal models to target glioblastoma multiforme (GBM), which is characterized by high expression of IL13Ralpha2. Patient-derived IL13-zetakine/HyTK expressing CD8+ CTL clones have entered early stage clinical trials. However, their clinical application is frequently limited in this patient population by the pervasive use of dexamethasone, a potent glucocorticoid analogue employed in the management of cerebral edema. Thus iatrogenic dexamethasone-mediated T-cell functional anergy and apoptosis in these patients is a barrier to realizing the full clinical utility of this adoptive therapy strategy. We hypothesized that knocking out the expression of the glucocorticoid receptor would render therapeutic CTLs resistant to the effects of synthetic glucocorticoids, including dexamethasone. We therefore developed engineered zinc finger nucleases (ZFNs) to specifically disrupt the glucocorticoid receptor (GR) locus in the human genome. ZFNs include the cleavage domain of the restriction enzyme FokI linked to an engineered zinc finger DNA-binding domain and can be designed to cleave a predetermined site in the genome: Natural repair of such DNA breaks via the error-prone non-homologous end joining pathway results in the inactivation of the target gene at frequencies which permit the isolation of knock out clones. Employing adenovirally

delivered and transiently expressed ZFNs targeting exon 3 of the human GR gene, we isolated IL13-zetakine+ CD8+T-cells containing a biallelically mutated GR locus. These cells were characterized by the absence of full length GR proteins lack of glucocorticoid hormone-induced gene regulation and resistance to glucocorticoid hormone-mediated immunosupression and apoptosis. Importantly, the ZFN-modified, glucocorticoid-resistant CTLs demonstrated zetakine re-directed cytolytic activity and tumor cell specificity in chromium release assays in vitro and in an orthotopic mouse model of GBM in vivo. These results indicate that glucocorticoid-resistant IL13-zetakine targeted CTLs should retain function in cancer patients receiving glucocorticoids. A clinical trial to test this hypothesis is currently under development.

L4 ANSWER 18 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2006:242500 USPATFULL
TITLE: Custom-made meganuclease and use thereof
INVENTOR(S): Arnould, Sylvain, 116 RUE LAMARCK, PARIS, FRANCE 75018
Bruneau, Slyvia, Paris, FRANCE
Cabaniols, Jean-Pierre, Saint Leu La Foret, FRANCE
Chames, Patrick, Paris, FRANCE
Choulika, Andre, Paris, FRANCE
Duchateau, Philippe, Cemy, FRANCE
Epinat, Jean-Charles, Paris, FRANCE
Gouble, Agnes, Paris, FRANCE
Lacroix, Emmanuel, Paris, FRANCE
Pagues, Frederic, Bourg La Reine, FRANCE
Smith, Julianne, Paris, FRANCE
Perez-Michaut, Christophe, Paris, FRANCE

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006206949	A1	20060914	
APPLICATION INFO.:	US 2004-543556	A1	20040128	(10)
	WO 2004-IB827		20040128	
			20060314	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-442911P	20030128 (60)
	US 2003-491535P	20030801 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NIXON & VANDERHYE, PC, 901 NORTH GLEBE ROAD, 11TH FLOOR, ARLINGTON, VA, 22203, US
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1-40
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 3834
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB New rare-cutting endonucleases, also called custom-made meganucleases, which recognize and cleave a specific nucleotide sequence, derived polynucleotide sequences, recombinant vector cell, animal, or plant comprising said polynucleotide sequences, process for producing said rare-cutting endonucleases and any use thereof, more particularly, for genetic engineering, antiviral therapy and gene therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 19 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2006:221707 USPATFULL
TITLE: Targeted deletion of cellular DNA sequences
INVENTOR(S): Guschin, Dmitry, Albany, CA, UNITED STATES

Holmes, Michael C., Oakland, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006188987	A1	20060824
APPLICATION INFO.:	US 2005-304981	A1	20051215 (11)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2004-912932, filed on 6 Aug 2004, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-649515P	20050203 (60)
	US 2003-493931P	20030808 (60)
	US 2003-518253P	20031107 (60)
	US 2003-530541P	20031218 (60)
	US 2004-542780P	20040205 (60)
	US 2004-556831P	20040326 (60)
	US 2004-575919P	20040601 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SANGAMO BIOSCIENCES, INC., 501 CANAL BOULEVARD, SUITE A100, RICHMOND, CA, 94804, US
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 3269
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein are methods and compositions for targeted deletion of double-stranded DNA. The compositions include fusion proteins comprising a cleavage domain (or cleavage half-domain) and an engineered zinc finger domain, and polynucleotides encoding same. Methods for targeted deletion include introduction of such fusion proteins, or polynucleotides encoding same, into a cell such that two targeted cleavage events occur. Subsequent cellular repair mechanisms result in deletion of sequences between the two cleavage sites.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 20 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2006:181431 USPATFULL
TITLE: Use of meganucleases for inducing homologous recombination ex vivo and in toto in vertebrate somatic tissues and application thereof
INVENTOR(S): Arnould, Sylvain, Paris, FRANCE
Bruneau, Sylvia, Paris, FRANCE
Cabaniols, Jean-Pierre, Saint Leu La Foret, FRANCE
Chames, Patrick, Paris, FRANCE
Choulika, Andre, Paris, FRANCE
Duchateau, Philippe, Cerny, FRANCE
Epinat, Jean-Charles, Paris, FRANCE
Gouble, Agnes, Paris, FRANCE
Lacroix, Emmanuel, Paris, FRANCE
Paques, Frederic, Bourg La Reine, FRANCE
Perez-Michaut, Christophe, Paris, FRANCE
Smith, Julianne, Paris, FRANCE
Sourdive, David, Levallois-Perret, FRANCE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006153826	A1	20060713
APPLICATION INFO.:	US 2004-543557	A1	20040128 (10)
	WO 2004-IB848		20040128

20060314 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-491535P	20030801 (60)
	US 2003-442911P	20030128 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: NIXON & VANDERHYE, PC, 901 NORTH GLEBE ROAD, 11TH FLOOR, ARLINGTON, VA, 22203, US
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1-18
NUMBER OF DRAWINGS: 20 Drawing Page(s)
LINE COUNT: 3298
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Use of meganucleases for inducing homologous recombination ex vivo and in toto in vertebrate somatic tissues and to its application for genome engineering and gene therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 22 OF 60 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE
ACCESSION NUMBER: 2006010180 ESBIOBASE
TITLE: Mammalian gene targeting with designed zinc finger nucleases
AUTHOR: Porteus M.H.
CORPORATE SOURCE: M.H. Porteus, Department of Pediatrics, University of Texas Southwestern Medical School, 5323 Harry Hines Boulevard, Dallas, TX 75390-9063, United States. E-mail: matthew.porteus@utsouthwestern.edu
SOURCE: Molecular Therapy, (2006), 13/2 (438-446), 40 reference(s)
CODEN: MTOHCK ISSN: 1525-0016
PUBLISHER ITEM IDENT.: S1525001605015558
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Gene targeting by homologous recombination is a powerful method to manipulate the genome precisely and could be exploited to correct genetic defects. Zinc finger nucleases are designed proteins that fuse a zinc finger DNA binding domain to the nuclease domain from the FokI restriction endonuclease. Zinc finger nucleases were generated that stimulated gene targeting from half-site sequences from the human β-globin gene and the human common γ-chain gene. Zinc finger nucleases were also generated that stimulated gene targeting at full sites from the green fluorescent protein gene and the human CD8α gene. This work built on the prior zinc finger design work of others and in targeting these four genes had a 100% success rate at designing nucleases to the consensus half-site 5'-GNNGNNGNN-3' and the consensus full site 5'-NNCNNCNNCNNNNNNGNNGNNGNN-3', suggesting that zinc finger nucleases can be empirically designed to stimulate gene targeting in a large portion of the mammalian genome. Copyright .COPYRGT. The American Society of the Gene Therapy.

L4 ANSWER 26 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2005:305926 USPATFULL

TITLE: Novel lentiviral vectors for site-specific gene insertion
INVENTOR(S): Yee, Jiing-Kuan, Arcadia, CA, UNITED STATES
Michel, Gilles H., Galveston, TX, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005266565	A1	20051201	
APPLICATION INFO.:	US 2005-121354	A1	20050503	(11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-567952P	20040503 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PERKINS COIE LLP, POST OFFICE BOX 1208, SEATTLE, WA, 98111-1208, US
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 1281
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Murine leukemia virus (MLV) and lentivirus vectors have been used previously to deliver genes to hematopoietic stem cells (HSCs) in human gene therapy trials. However, these vectors integrate randomly into the host genome, leading to disruption or inactivation of vital host genes. The present invention discloses a novel lentiviral vector system that overcomes this problem by integrating into a host genome in a site-specific manner.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 27 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2005:298923 USPATFULL
TITLE: In vivo ssdna expression vectors for altering gene expression
INVENTOR(S): Conrad, Charles A., Houston, TX, UNITED STATES
Chen, Yin, Pearland, TX, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005260588	A1	20051124	
APPLICATION INFO.:	US 2003-513191	A1	20030501	(10)
	WO 2003-US13593		20030501	
			20050711	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-10136218	20020501

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Mark R Wisner, Wisner & Associates, 1177 West Loop South, Suite 400, Hoston, TX, 77027-9012, US
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1733
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An expression vector for altering expression of a target nucleic acid sequence in a host cell by production of single-stranded cDNA (ssDNA) in the host cell in vivo. The expression vector is comprised of a cassette comprising a sequence of interest, an inverted tandem repeat, and a

primer binding site 3' to the inverted tandem repeat, and a reverse transcriptase/RNAse H coding gene, and may be transfected into the host cell. Transcription of the cassette by the host cell produces an RNA template which is reverse transcribed with the product of the RT coding gene to produce ssDNA of a specified sequence. The ssDNA is modified to remove flanking vector sequences by taking advantage of the "stem-loop" structure of the ssDNA, which forms as a result of the inverted tandem repeat that allows the ssDNA to fold back on itself, forming a double stranded DNA stem. The double-stranded stem may contain one or more restriction endonuclease recognition sites and the loop, which remains as ssDNA, can be any desired nucleotide sequence. This design allows the double-stranded stem of the stem-loop intermediate to be cleaved by the desired corresponding restriction endonuclease(s) and the loop portion is then released as a linearized, single-stranded piece of DNA. The resulting ssDNA binds to an endogenous target nucleic acid sequence to alter the expression of that sequence for such therapeutic purposes as gene activation or inactivation using duplex or triplex binding of nucleic acids, site-directed mutagenesis, interruption of cellular function by binding to specific cellular proteins, or interfering with RNA splicing functions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 35 OF 60 USPATFULL on STN

ACCESSION NUMBER: 2004:25160 USPATFULL

TITLE: Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site

INVENTOR(S): Choulika, Andre, Paris, FRANCE
Mulligan, Richard C., Lincoln, MA, UNITED STATES

PATENT ASSIGNEE(S): The Children's Medical Center Corporation, Boston, MA (non-U.S. corporation)
The Institute Pasteur, Paris, FRANCE (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004019002	A1	20040129
APPLICATION INFO.:	US 2003-337229	A1	20030106 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-917295, filed on 27 Jul 2001, ABANDONED Continuation of Ser. No. WO 2000-US3014, filed on 3 Feb 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-118669P	19990203 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133

NUMBER OF CLAIMS: 52

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 6 Drawing Page(s)

LINE COUNT: 1130

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell are disclosed. Also disclosed are methods of treating or prophylaxis of a genetic disease in an individual in need thereof. Further disclosed are chimeric restriction endonucleases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 36 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-14313 BIOTECHDS
TITLE: New chimeric nuclease comprising a DNA binding domain, a cleavage domain and a nuclear localization signal, useful in preparing a composition for treating or preventing a genetic disease e.g., hemophilia or Huntington's disease; vector-mediated DNA binding protein gene transfer and expression in host cell for recombinant vaccine
AUTHOR: BALTIMORE D; PORTEUS M
PATENT ASSIGNEE: CALIFORNIA INST OF TECHNOLOGY
PATENT INFO: WO 2004037977 6 May 2004
APPLICATION INFO: WO 2003-US27958 5 Sep 2003
PRIORITY INFO: US 2003-484788 3 Jul 2003; US 2002-408454 5 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-365503 [34]
AN 2004-14313 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A new chimeric nuclease comprises a DNA binding domain, a cleavage domain and a nuclear localization signal.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a complex comprising a first chimeric nuclease and a second chimeric nuclease, each comprising cleavage and DNA binding domains; (2) a nucleic acid encoding a chimeric nuclease; (3) a vector comprising the nucleic acid; (4) a cell comprising the vector; (5) a recombinant transfection system comprising the vector and a gene delivery composition for delivering the vector to a cell and causing the cell to be transfected with the vector; (6) a method of changing a target sequence in genomic DNA of a mammalian cell; (7) a method for ameliorating, treating or preventing a disease caused, in part or in whole, by a genomic target sequence; and (8) a method of designing a nucleic acid encoding a chimeric nuclease.

BIOTECHNOLOGY - Preferred Nuclease: The DNA binding domain binds to a recognition sequence comprising at least 6 or 9 designated nucleotides. It comprises three or more zinc finger domains. The recognition sequence occurs at a position in a mammalian genome within at least 500 bp of an allele that contributes to a genetic disorder. The cleavage domain comprises a cleavage domain of a type IIs or FokI restriction endonuclease. Preferred Vector: The vector is a viral vector. The promoter is an inducible promoter. Preferred Nucleic Acid: The nucleic acid is operably linked to a promoter for expression in a mammalian cell. The nucleic acid comprises a repair substrate. Preferred Cell: The cell is a mammalian cell. It is a human cell. It is an in vitro cell. Preferred Method: Changing a target sequence in genomic DNA of a mammalian cell comprises introducing a chimeric nuclease into the cell; and introducing the repair substrate into the cell, where the target sequence is changed by the repair substrate upon recombination. The target sequence contains an allele that contributes to a disease that is repaired by the repair substrate. It is situated in a gene that is attenuated or inactivated by the repair substrate. It is replaced by a heterologous sequence in the repair substrate. Introducing the chimeric nuclease into the cell comprises introducing a nucleic acid encoding the chimeric nuclease into the cell. The nucleic acid encoding the chimeric nuclease and the repair substrate are present in a single vector introduced into the cell. The chimeric nuclease protein is introduced into the cell as a protein. The chimeric nuclease forms a homodimer of two identical or different chimeric nucleases. Ameliorating, treating or preventing a disease caused,

in part or in whole, by a genomic target sequence comprises introducing a chimeric nuclease into a cell and introducing a repair substrate in the cell. The cell is reintroduced into the individual after the target sequence is altered. The cell is a stem cell or a population of cells comprising the stem cell. The cell is an in vitro cell obtained from a donor or an in vivo cell in the individual. The disease comprises severe combined immunodeficiency, sickle cell disease or hemophilia. The disease is an infectious disease, comprising HIV infection. The genomic target sequence is at least a portion of a gene for a cell surface protein that participates in cell entry by HIV. Altering the target sequence inhibits cell entry by HIV. The cell is a T cell or T cell progenitor. Designing a nucleic acid encoding a chimeric nuclease comprises: (1) selecting a mammalian target sequence for gene targeting; (2) identifying a possible DNA binding sequence within workable proximity of the target sequence; (3) designing a nucleic acid encoding a DNA binding domain that binds to the DNA binding sequence identified in (2); and (4) coupling the nucleic acid encoding the DNA binding domain in (3) to a nucleic acid encoding a cleavage domain to make a nucleic acid comprising the coding sequence for the chimeric nuclease. The method further comprises selecting a second possible DNA binding sequence within workable proximity of the target sequence and positioned so that a chimeric nuclease bound to the second possible DNA binding sequence acts conjointly with a chimeric nuclease bound to the possible DNA binding sequence of (2) and generating a nucleic acid encoding a chimeric nuclease that binds to the second possible DNA binding sequence. The method further comprises coupling a nucleic acid encoding a nuclear localization signal to the nucleic acid comprising the coding sequence for the chimeric nuclease. The DNA binding domain comprises a zinc finger-binding domain. The method further comprises testing the chimeric enzyme for toxicity in a cell and testing the cleavage site specificity of the chimeric enzyme.

ACTIVITY - Hemostatic; Muscular-Gen; Nootropic. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The chimeric nuclease is useful in preparing a composition for treating or preventing a genetic disease e.g., hemophilia, Tay-Sachs disease, Huntington's disease, Duchenne's muscular dystrophy or Lesch Nylan syndrome.

ADMINISTRATION - The composition is administered via oral or parenteral route. No dosage given.

EXAMPLE - No relevant examples given. (85 pages)

L4 ANSWER 40 OF 60 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
DUPLICATE 16

ACCESSION NUMBER: 2003-28335 BIOTECHDS
TITLE: Targeted genetic recombination in a host cell comprises introducing into a host cell a nucleic acid molecule encoding a Zinc Finger Nuclease (ZFN), inducing expression of the ZFN, and identifying a host cell exhibiting a mutation; vector-mediated zinc finger nuclease gene transfer and expression in plant or animal host cell for gene therapy or agriculture
AUTHOR: CARROLL D; BIBIKOVA M; DREWS G N; GOLIC K G; GOLIC M M
PATENT ASSIGNEE: UNIV UTAH RES FOUND
PATENT INFO: WO 2003087341 23 Oct 2003
APPLICATION INFO: WO 2003-US2012 22 Jan 2003
PRIORITY INFO: US 2002-351035 23 Jan 2002; US 2002-351035 23 Jan 2002
DOCUMENT TYPE: Patent

LANGUAGE: English
OTHER SOURCE: WPI: 2003-833726 [77]
AN 2003-28335 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Targeted genetic recombination in host cell comprises introducing into a host cell a nucleic acid molecule encoding a Zinc Finger Nuclease (ZFN) targeted to a chosen host target locus, inducing expression of the ZFN within the host cell, and identifying a host cell in which the selected host DNA sequence exhibits a mutation at the host target locus.

BIOTECHNOLOGY - Preferred Method: In targeted genetic recombination in a host cell, the mutation is a deletion and/or an insertion of a genetic material. The method further comprises introducing donor DNA into the host cell, where the donor DNA provides a gene sequence that encodes a product to be produced in the host cell. The product is selected from pharmaceuticals, hormones, proteins, nutriceuticals or chemicals. The host cell is a single celled organism or is a cell from a multicellular organism. The cell is an oocyte. The host cell is an insect cell. The insect is a member of an order selected from Coleoptera, Diptera, Hemiptera, Homoptera, Hymenoptera, Lepidoptera or Orthoptera. The insect is a fruit fly, a mosquito or a medfly. The organism is a monocotyledon plant selected from maize, rice or wheat. Alternatively, the plant is a dicotyledon plant selected from potato, soybean, tomato, members of the Brassica family or Arabidopsis. The plant may also be a tree. The organism may also be a mammal, a bird or a fish. The mammal is selected from mouse, rat, pig, sheep, cow, dog or cat. The bird is chicken, turkey, duck or goose. The fish is a zebrafish, trout or salmon. The mutation occurs in a germ line cell or in a somatic cell of the organism. Alternatively, the method comprises selecting a zinc finger DNA binding domain capable of preferentially binding to a specific host target locus to be mutated, selecting a non-specific DNA cleavage domain capable of cleaving double-stranded DNA when operatively linked to the binding domain and introduced into the host cell, selecting an inducible control element capable of inducing expression in the host cell, operatively linking the DNA encoding the binding domain and the cleavage domain and the inducible control element to produce a DNA construct, introducing the DNA construct into a target host cell, and identifying at least one host cell exhibiting recombination at the target locus in the host DNA. The method further comprises introducing the donor DNA cited above into the host cell. The DNA binding domain is comprised of three zinc fingers. The zinc fingers are selected from Cis2His2zinc fingers. The cleavage domain is selected from Type II restriction endonucleases. The Type II restriction endonuclease is FokI. The inducible control element is selected from heat-shock inducible control elements. The target cell is a gamete cell of the host organism. The DNA construct further comprises DNA encoding one or more selectable marker(s). The selectable marker provides positive and/or negative selection for cells expressing the marker.

USE - The method is useful for targeted genetic recombination or mutagenesis in a host cell or organism. The method may be utilized for therapeutic or agricultural purposes.

ADVANTAGE - The method is generally applicable to a wide variety of organisms, as compared with other conventional techniques. It is efficient and inexpensive to perform and is adaptable to any cell or organism. The method is targeted so that the disadvantages associated with random insertion of DNA into a host genetic material are eliminated, and that certain embodiments require relatively little manipulation of the host genetic material. (42 pages)

L4 ANSWER 41 OF 60 USPATFULL on STN

ACCESSION NUMBER: 2003:330199 USPATFULL
TITLE: Methods and compositions for using zinc finger endonucleases to enhance homologous recombination
INVENTOR(S): Liljedahl, Monika, La Jolla, CA, UNITED STATES
Aspland, Simon Eric, San Diego, CA, UNITED STATES
Segal, David J., Tucson, AZ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003232410	A1	20031218
APPLICATION INFO.:	US 2003-395816	A1	20030320 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-367114P	20020321 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614
NUMBER OF CLAIMS: 36
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 1481
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Embodiments relate to methods of generating a genetically modified cell. The methods can include providing a primary cell containing an endogenous chromosomal target DNA sequence in which it is desired to have homologous recombination occur. The methods also can include providing a zinc finger endonuclease (ZFE) that includes an endonuclease domain that cuts DNA, and a zinc finger domain that includes a plurality of zinc fingers that bind to a specific nucleotide sequence within the endogenous chromosomal target DNA in the primary cell. Further, the methods can include contacting the endogenous chromosomal target DNA sequence with the zinc finger endonuclease in the primary cell such that the zinc finger endonuclease cuts both strands of a nucleotide sequence within the endogenous chromosomal target DNA sequence in the primary cell, thereby enhancing the frequency of homologous recombination in the endogenous chromosomal target DNA sequence. The methods also include providing a nucleic acid comprising a sequence homologous to at least a portion of said endogenous chromosomal target DNA such that homologous recombination occurs between the endogenous chromosomal target DNA sequence and the nucleic acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 51 OF 60 USPATFULL on STN
ACCESSION NUMBER: 2002:199105 USPATFULL
TITLE: Gene repair involving the induction of double-stranded DNA cleavage at a chromosomal target site
INVENTOR(S): Choulika, Andre, Paris, FRANCE
Mulligan, Richard C., Lincoln, MA, UNITED STATES
PATENT ASSIGNEE(S): The Children's Medical Center, Boston, MA, UNITED STATES (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002107214	A1	20020808
APPLICATION INFO.:	US 2001-917295	A1	20010727 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 2000-US3014, filed on 3 Feb 2000, UNKNOWN		

	NUMBER	DATE

PRIORITY INFORMATION:	US 1999-118669P 19990203 (60)
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS:	52
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	6 Drawing Page(s)
LINE COUNT:	1128

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell are disclosed. Also disclosed are methods of treating or prophylaxis of a genetic disease in an individual in need thereof. Further disclosed are chimeric restriction endonucleases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 53 OF 60 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER:	2003:357643 BIOSIS
DOCUMENT NUMBER:	PREV200300357643
TITLE:	Chimeric Nucleases Stimulate Gene Targeting in Human Cells.
AUTHOR(S):	Porteus, Matthew [Reprint Author]; Baltimore, David [Reprint Author]
CORPORATE SOURCE:	Biology, California Institute of Technology, Pasadena, CA, USA
SOURCE:	Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 821. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE:	Conference; (Meeting) Conference; (Meeting Poster) Conference; Abstract; (Meeting Abstract)
LANGUAGE:	English
ENTRY DATE:	Entered STN: 6 Aug 2003 Last Updated on STN: 6 Aug 2003

AB Gene targeting is a powerful technique to introduce genetic change into the genome of eukaryotic cells. It is widely used to create defined mutations in murine embryonic stem cells and theoretically could be used to create or repair mutations in somatic cells. In this way gene targeting could be a powerful form of gene correction type gene therapy. Despite its potential, gene targeting has not been widely used in somatic cells because of its low efficiency. We report on a system based on the correction of a mutated GFP gene that allows the efficient study of gene targeting in somatic cells. Using this system we show that gene targeting is stimulated over 2000-fold by the introduction of a DNA double-stranded break in the target locus (DSB-GT). We find that the rate of DSB-GT can be increased by increasing the amount of repair substrate, the amount of homology between the gene target and repair substrate, and by increasing the frequency of double-stranded break creation. When we optimize conditions for DSB-GT we obtain targeting rates of 3-5%. Finally, we show that chimeric nucleases, protein fusions between zinc finger DNA binding domains and the endonuclease domain of the FokI restriction enzyme, can stimulate gene targeting in the genome of human somatic cells by several-thousand fold. Our data provides a paradigm for the use of gene targeting as a form of gene therapy for monogenic diseases.

L4 ANSWER 56 OF 60 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:553718 CAPLUS
DOCUMENT NUMBER: 133:160582
TITLE: Gene repair involving homologous recombination induced by in vivo double-stranded cleavage of targeting DNA mediated by chimeric restriction endonuclease
INVENTOR(S): Choulika, Andre; Mulligan, Richard C.
PATENT ASSIGNEE(S): Children's Medical Center Corporation, USA; Institute Pasteur
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000046386	A2	20000810	WO 2000-US3014	20000203
WO 2000046386	A3	20001214		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2361191	A1	20000810	CA 2000-2361191	20000203
EP 1147209	A2	20011024	EP 2000-908499	20000203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002535995	T	20021029	JP 2000-597445	20000203
US 20020107214	A1	20020808	US 2001-917295	20010727
US 20040019002	A1	20040129	US 2003-337229	20030106
US 20070141038	A1	20070621	US 2006-636397	20061208

PRIORITY APPLN. INFO.:		
US 1999-118669P	P	19990203
WO 2000-US3014	W	20000203
US 2001-917295	B1	20010727
US 2003-337229	B1	20030106

AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell through chimeric restriction endonuclease (or meganuclease)-induced homologous recombination are disclosed. 101The method is exemplified by introducing into a cell a vector containing a targeting DNA homologous to a chromosomal target sites and is flanked by specific sites for restriction endonuclease I-SceI (a Saccharomyces cerevisiae intron-encoded rare-cutter endonuclease recognizing 18-bp sequence) or meganuclease, and cDNA encoding I-SceI or meganuclease. The I-SceI site is recognized and cleaved in vivo to relase the repair matrix and induce homologous recombination. The method has applications in treating or prophylaxis of a genetic disease in an individual in need.

=> d his full

(FILE 'HOME' ENTERED AT 01:36:11 ON 08 MAY 2008)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 01:36:38 ON 08 MAY 2008
SEA GENE?(S)TARGET?(S)(RECOMBINAS? OR ENDONUCLEAS? OR NUCLEAS?

26	FILE ADISINSIGHT
9	FILE ADISNEWS
368	FILE AGRICOLA
15	FILE ANABSTR

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              13   FILE ANTE
               6   FILE AQUALINE
              58   FILE AQUASCI
             677   FILE BIOENG
             661   FILE BIOSIS
            1838   FILE BIOTECHABS
            1838   FILE BIOTECHDS
            1942   FILE BIOTECHNO
             603   FILE CABA
            1467   FILE CAPLUS
              50   FILE CEABA-VTB
              18   FILE CIN
              12   FILE CONFSCI
               4   FILE CROPU
              65   FILE DDFU
           74883   FILE DGENE
             383   FILE DISSABS
             136   FILE DRUGU
               8   FILE EMBAL
             530   FILE EMBASE
            2812   FILE ESBIOBASE
              18   FILE FROSTI
              53   FILE FSTA
             411   FILE GENBANK
               7   FILE HEALSAFE
            1311   FILE IFIPAT
              45   FILE IMSDRUGNEWS
              25   FILE IMSRESEARCH
              15   FILE KOSMET
            2522   FILE LIFESCI
             591   FILE MEDLINE
              51   FILE NTIS
               2   FILE NUTRACEUT
              10   FILE OCEAN
             924   FILE PASCAL
               2   FILE PHAR
               3   FILE PHARMAML
              27   FILE PHIN
             314   FILE PROMT
             655   FILE SCISEARCH
               3   FILE SYNTHLINE
             356   FILE TOXCENTER
            7702   FILE USGENE
           11946   FILE USPATFULL
              43   FILE USPATOLD
            1592   FILE USPAT2
              11   FILE WATER
             815   FILE WPIDS
              19   FILE WPIFV
             815   FILE WPINDEX
               7   FILE IPA
             193   FILE NLDB
L1               QUE GENE?(S) TARGET?(S)(RECOMBINAS? OR ENDONUCLEAS? OR
                 NUCLEAS? OR ZINC?)
                 ---------
                 D RANK

     FILE 'USPATFULL, USGENE, ESBIOBASE, LIFESCI, BIOTECHNO, BIOTECHDS,
     USPAT2, CAPLUS, IFIPAT, PASCAL, WPIDS, BIOENG, BIOSIS, SCISEARCH, CABA,
     MEDLINE' ENTERED AT 01:41:10 ON 08 MAY 2008
L2          38060 SEA GENE?(S) TARGET?(S)(RECOMBINAS? OR ENDONUCLEAS? OR
                  NUCLEAS? OR ZINC?)
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L3           89 SEA L2(S) FOK?(S) BINDIN?
L4           60 DUP REM L3 (29 DUPLICATES REMOVED)
                D TI L4
                D TI L4 1-60
                D IBIB ABS L4 2-7,10,15,18-20,22,26-27,35-36,40-41,51,53,56


      FILE HOME

      FILE STNINDEX

      FILE USPATFULL
      FILE COVERS 1971 TO PATENT PUBLICATION DATE: 6 May 2008 (20080506/PD)
      FILE LAST UPDATED: 6 May 2008 (20080506/ED)
      HIGHEST GRANTED PATENT NUMBER: US7370367
      HIGHEST APPLICATION PUBLICATION NUMBER: US2008104734
      CA INDEXING IS CURRENT THROUGH 6 May 2008 (20080506/UPCA)
      ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 6 May 2008 (20080506/PD)
      REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2008
      USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2008


      FILE USGENE
      FILE LAST UPDATED:            2 MAY 2008       <20080502/UP>
      MOST RECENT PUBLICATION DATE: 1 MAY 2008       <20080501/PD>

      FILE COVERS 1982 TO DATE

      >>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION (SLART) IS AVAILABLE
          IN THE BASIC INDEX (/BI) AND FEATURE TABLE (/FEAT) FIELDS <<<

      >>> FOR THE LATEST USGENE REFERENCE MATERIALS, PLEASE VISIT:
      http://www.stn-international.com/stndatabases/details/usgene-first-p.html

      >>> DOWNLOAD RUN BLAST/GETSIM FREQUENTLY ASKED QUESTIONS:
      http://www.stn-international.com/training_center/bioseq/usgenefaq.pdf

      >>> DOWNLOAD COMPLETE USGENE HELP AS PDF:
      http://www.stn-international.com/training_center/bioseq/usgene_help.pdf <<

      >>> USGENE now provides USPTO sequence data within 3 days of publication
          - see NEWS <<<

      >>> SEARCH AND DISPLAY OF USPTO EXEMPLARY CLAIM (ECLM) IS AVAILABLE !! <<<

      FILE ESBIOBASE
      FILE LAST UPDATED: 6 MAY 2008       <20080506/UP>
      FILE COVERS 1994 TO DATE.

      >>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
           /CC, /ORGN, AND /ST  <<<

      FILE LIFESCI
      FILE COVERS 1978 TO 1 May 2008 (20080501/ED)

      FILE BIOTECHNO
      FILE LAST UPDATED: 7 JAN 2004       <20040107/UP>
      FILE COVERS 1980 TO 2003.
      THIS FILE IS A STATIC FILE WITH NO UPDATES

      >>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
           /CT AND BASIC INDEX  <<<
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